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10/575,099	02/06/2007	Shuji Terashima	P29763	9412

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EXAMINER	
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1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/575,099	TERASHIMA ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *19-29 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 30-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/22/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 19-29 and 34 have been withdrawn.

Claims 1-18 and 30-33 are under examination.

2. The objections to claims 8 and 12 are withdrawn in response to Applicant's arguments field on 12/08/2008.

Response to Arguments

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-18 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 12-17 of U.S. Patent No. 6,268,119 in view of each Oka et al. (U.S. Patent NO 5,298,165), Oka et al. (PGPUB 2004/0251195, Applicant's IDS), Fukuda et al. (WO 02/087660, Abstract, Applicant's IDS), and Rubinstein et al. (Proc Natl Acad Sci USA, 1995, 92: 10119-10112, Applicant's IDS).

The instant claims are drawn to a method of preparing a concentrate of nucleated cells by introducing a cell-containing solution which contains both nucleated cells and unnecessary cells into a filter device comprising an inlet and an outlet, wherein the filter device capture the nucleated cells and discharges the unnecessary cells, followed by the addition of a recovery solution to recover the nucleated cells captured by the filter; before being introduced into the filter device, the cell-containing solution is separated into a layer rich in nucleated cells, a nucleated cell-diluted layer (i.e., plasma), and a layer rich in unnecessary cells, wherein the layer rich in unnecessary cells is the first to be introduced into the filter device, followed by nucleated cell-diluted layer and the layer rich in nucleated cells in this order; the recovery solution could be the nucleated cell-diluted layer (i.e., plasma) and the recovery solution is further centrifuged to concentrate the nucleated cells (claims 1, 7-10, and 30-33). Separation of the cell-containing solution into layers takes place by centrifugation or by agglutination with hydroxyethyl starch (HES) followed by centrifugation (claims 2, 3, and 6), the unnecessary cells are erythrocytes, and the nucleated cells are hematopoietic stem cells (claims 4 and 5). The filter device further contains an aggregate-capturing

material between the inlet and the filter and a porous recovery solution-rectifying material between the filter and the outlet; the filter and the recovery solution-rectifying material form a porous filter material wherein the value obtained by dividing the effective filtration area of the filter material by the thickness of the nucleated cell-capturing filter is between 15 and 120 cm (claims 11-13). The filter material is non-woven fabric (having an average fiber diameter of 1.1-3.0 μm for the cell-capturing material or 0.5-1.5 μm for the rectifying material, with a packaging density of 0.1-0.3 g/cm^3), a sponge-like structure (having an average pore diameter of 7-25 μm for the cell-capturing material or of 2-10 μm for the rectifying material, with a porosity between 55 and 90%), or a combination of a non-woven fabric with a sponge-like structure (claims 14-18).

The patent claims recite a cell separation method comprising introducing a fluid containing cells to be recovered and cells to be removed into a cell-capturing device having an inlet and an outlet and a cell-capturing means which captures the cells to be recovered and discharges the cells to be removed, followed by the introduction of a liquid into the cell-capturing means to recover the captured cells; the cell-capturing means comprises non-woven fabrics with a fiber diameter of 1.0-30 μm or porous spongy structure having a pore size of 2.0-25 μm (claims 1, 6, and 12). The cells to be recovered are nucleated cells such as hematopoietic stem cells and the cells to be removed are erythrocytes (claims 13-17). The specification defines that the liquid used to recover the captured cells could be plasma (p. 8, lines 21-51, p. 12, line 63 through lines 1-5 of p. 13). The patent claims do not recite a composite filter comprising an aggregate-capturing material, a nucleated cell-capturing material, and a recovery

solution rectifying material, nor do they recite using centrifugation to separate the cell-containing solution into a layer rich in nucleated cells, a nucleated cell-diluted layer, and a layer rich in unnecessary cells before introducing it into the filter device or adding HES before centrifuging the cell-containing solution. However, at the time the invention was made, such limitations were well known and used in the prior art. For example, Oka et al. (U.S. Patent NO 5,298,165) teach improved leukocyte capturing by using a composite filter comprising a pre-filter (i.e., an aggregate-capturing material), a nucleated cell-capturing filter, and a microfilter, in this order (Abstract, column 8, lines 25-45, column 10, lines 19-30 and 62-67, column 11, lines 1-16). It is noted that the instant specification defines the recovery solution rectifying material as a porous filter having a packing density of 0.1-0.3 g/cm^3 and an average fiber diameter of 0.5-1.5 μm (p. 19, second full paragraph). Since Oka et al. (U.S. Patent NO 5,298,165) teach their microfilter as having a packing density of 0.15-0.38 g/cm^3 and a fiber diameter of 0.5-1.4 μm (column 8, lines 60-66, column 12, lines 53-55), their microfilter has the same properties as the claimed recovery solution rectifying material, i.e., their microfilter is a recovery solution rectifying material. In addition, both Oka et al. (PGPUB 2004/0251195) and Fukuda et al. teach a method for isolating nucleated cell from blood, the method comprising centrifuging the blood, i.e., separating the blood into a buffy coat (layer rich in nucleated cells), plasma (nucleated cell-diluted layer), and an erythrocyte pellet (layer rich in unnecessary cells), followed by introducing the separated blood into a filter device, wherein such a separation results in high retention of nucleated cells on the filter (see Oka et al., p. 1, paragraphs 0005 and 0010; Fukuda et al., Abstract).

Rubinstein et al. teach adding HES to blood to enhance erythrocyte sedimentation (p. 10120, column 2, third paragraph). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the patent claims by introducing the HES/centrifugation steps and using a composite filter as taught by the prior art, with a reasonable expectation of success. One of skill in the art would have been motivated to do so because the art teaches that such modifications result in increased retention of nucleated cells within the filter device. With respect to the different values recited in the instant claims 11, 12, 15, and 17, it would have been obvious to one of skill in the art to vary the parameters (i.e., fiber or pore size and packaging density) to optimize the results according to the nucleated cell to be separated. With respect to centrifuging the recovery solution, it would have been obvious to one of skill in the art to do such in order to further concentrate the recovered nucleated cells. With respect to using a combination between a non-woven and a sponge-like material, it would have been obvious to one of skill in the art to do so in order to improve the performance of the filter device. With respect to the limitation of the recovery solution being nucleated cell diluted layer (i.e., plasma, see above), since the specification defines that the recovery solution could plasma, it would have been obvious to one of skill in the art to use such a layer to achieve the predictable result of recovering the nucleated cells. Thus, the instant claims and patent claims are obvious variants.

Applicant traversed the instant rejection on the grounds that the analysis misses the relevant question for obviousness-type double patenting, i.e., whether the claims are

obvious variants. Specifically, Applicant argues that a proper obviousness-type double patenting rejection should compare the claims of one application to the claims in another patent or application. Applicant submits that the Examiner appears to make the case for why the instant claims would be obvious over the prior art as a whole and not why they would be obvious over the earlier claims, i.e., the rejection fails to address this critical inquiry. Applicant also argues that the presently claimed invention is not obvious in view of the patent claims because none of the patent claims suggests the elements of claims 1 and 12. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

It is noted that an obviousness-type double patenting rejection can be made using secondary references (see MPEP 804). Therefore, even if the patent claims do not recite all elements of claims 1 and 12, these elements were obvious in view of the secondary references cited above. For these reasons, the rejection is maintained.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-17 and 30-33 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Sumita et al. (U.S. Patent No. 6,268,119), in view of each Oka et al. (U.S. Patent No. 5,298,165), Fukuda et al. (WO 02/087660), Oka et al. (PGPUB 2004/0251195), and Rubinstein et al. (Proc Natl Acad Sci USA, 1995, 92: 10119-10122).

Sumita et al. teach a method of preparing a nucleated cell concentrate by introducing blood into a filter device comprising a filter material capable of capturing nucleated cells and discharging unnecessary cells, followed by the introduction of a recovery solution to elute the captured nucleated cells; the filter material could be a non-woven fabric with a diameter of 1-30 μm or a spongy structure with a pore size of 3-20 μm, the nucleated cells are hematopoietic stem cells, the unnecessary cells are erythrocytes, and the recovery solution could be plasma (claims 1, 4, 5, 30, 32, and 33) (column 2, lines 51-67, column 3, lines 1-8 and 50-55, column 5, lines 18-67, column 6, lines 27-60, column 8, lines 21-51, p. 12, line 63 through lines 1-5 of p. 13).

Sumita et al. do not teach a composite porous filter material comprising, in a direction from the inlet to the outlet, an aggregate-capturing material, a nucleated cell-capturing material, and a recovery solution-rectifying material, wherein the filter material comprises a non-woven fabric, a sponge-like structure, or a combination between a non-woven fabric and a sponge-like structure (claims 11-17). Oka et al. (U.S. Patent NO 5,298,165) teach improved leukocyte capturing by using a porous composite filter made of a non-woven material comprising in the upstream to downstream order: a pre-filter (i.e., an aggregate-capturing material), a nucleated cell-capturing filter, and a

microfilter (Abstract, column 8, lines 25-45, column 10, lines 19-30 and 62-67, column 11, lines 1-16). The porous composite filter of Oka et al. (U.S. Patent NO 5,298,165) has an average fiber diameter of 1.0-2.0 μm for the nucleated cell-capturing material and of 0.5-1.4 μm for the microfilter material and a packing density of 0.15-0.38 g/cm^3 (claim 15) (column 8, lines 60-66, column 10, lines 19-30). With respect to the limitation of recovery solution rectifying material, it is noted that the instant specification defines the recovery solution rectifying material as a porous filter having a packing density of 0.1-0.3 g/cm^3 and an average fiber diameter of 0.5-1.5 μm (p. 19, second full paragraph). Since Oka et al. (U.S. Patent NO 5,298,165) teach their microfilter as having a packing density of 0.15-0.38 g/cm^3 and a fiber diameter of 0.5-1.4 μm (column 8, lines 60-66, column 12, lines 53-55), their microfilter has the same properties as the claimed recovery solution rectifying material, i.e., their microfilter is a recovery solution rectifying material. Therefore, Oka et al. (U.S. Patent NO 5,298,165) teach a porous composite filter comprising in a direction from the inlet to the outlet, an aggregate-capturing material, a nucleated cell-capturing material, and a recovery solution-rectifying material. It would have been obvious to one of skill in the art, at the time the invention was made, to modify the filter device of Sumita et al., by using the composite filter device of Oka et al. (U.S. Patent NO 5,298,165), with a reasonable expectation of success. The motivation to do so is provided by Oka et al. (U.S. Patent NO 5,298,165), who teach that composite filters are very efficient in removing nucleated cells from blood. One of skill in the art would have been expected to have a reasonable expectation of success in doing so because the art teaches that composite filters can be

successfully used to capture blood nucleated cells. With respect to the limitations recited in claim 17, Oka et al. (U.S. Patent NO 5,298,165) teach an average pore diameter of 6-20 μm for the nucleated cell-capturing material, of 4-12 μm for the recovery solution-rectifying material and a packing density of 0.15-0.38 g/cm^3 (column 10, lines 41-45, column 12, lines 53-55). Therefore, it would have been obvious to one of skill in the art, at the time the invention was made, to modify the sponge-like filter of Sumita et al. according to the teachings of Oka et al. (U.S. Patent NO 5,298,165) to achieve the predictable result of obtaining a composite sponge-like filter with improved properties.

Sumita et al. and Oka et al. (U.S. Patent NO 5,298,165) do not teach using centrifugation to separate the cell-containing solution into a layer rich in nucleated cells, a nucleated cell-diluted layer, and a layer rich in unnecessary cells before introducing it into the filter device or adding HES before centrifuging the cell-containing solution (claims 1-3 and 6-8). However, at the time the invention was made, such limitations were well known and used in the prior art. For example, both Oka et al. (PGPUB 2004/0251195) and Fukuda et al. teach a method for isolating nucleated cell from blood, the method comprising centrifuging the blood with the simultaneous introduction of the separated components into nucleated cell-capturing filters, wherein the method results in high retention of nucleated cells on the filter (see Oka et al., p. 1, paragraphs 0005 and 0010, p. 2, paragraph 0017; Fukuda et al., Abstract). Such a method would necessarily result in a cell gradient comprising a buffy coat at the top (layer rich in nucleated cells), plasma in the middle (nucleated cell-diluted layer), and an erythrocyte

pellet at the bottom (layer rich in unnecessary cells) with the introduction into the filter of the separated components in the order of erythrocyte pellet first, plasma second, and buffy coat third (claims 1, 7, and 8). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Sumita et al. and Oka et al. (U.S. Patent NO 5,298,165) by introducing into the filter device a blood cell gradient as taught by Fukuda et al. and Oka et al. (PGPUB 2004/0251195), with a reasonable expectation of success. The motivation to do so is provided by Fukuda et al., who teach that such a method results in high retention of nucleated cells on the filter (Abstract). One of skill in the art would have been expected to have a reasonable expectation of success in doing so because the art teaches that such steps can be successfully used to obtain nucleated cells from blood. Sumita et al., Oka et al. (U.S. Patent NO 5,298,165), Fukuda et al., and Oka et al. (PGPUB 2004/0251195) do not teach using HES in combination with centrifugation (claims 3 and 6). Rubinstein et al. teach adding HES to blood to enhance erythrocyte sedimentation (p. 10120, column 2, third paragraph). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Sumita et al., Oka et al. (U.S. Patent NO 5,298,165), Fukuda et al., and Oka et al. (PGPUB 2004/0251195) by introducing the HES before the centrifugation step, with a reasonable expectation of success. One of skill in the art would have been motivated to do so in order to improve separation of blood into its components. One of skill in the art would have been expected to have a reasonable expectation of success in doing so because the art teaches that HES improves erythrocyte elimination. With respect to the limitation of the filter having value

obtained by dividing the effective filtration area by the thickness of the nucleated cell-capturing material of 15-120 cm (claims 11 and 12) or of porosity of 55-90% (claim 17), it would have been obvious to one of skill in the art to use routine experimentation to vary these parameters to optimize the results according to the nucleated cell to be separated (see Oka et al., U.S. Patent NO 5,298,165, column 6, lines 3-9). With respect to centrifuging the recovery solution (claim 10), it would have been obvious to one of skill in the art to do such in order to further concentrate the recovered nucleated cells. With respect to the limitation of the recovery solution being nucleated cell diluted layer (claim 9), since Sumita et al. teach that plasma can be used s a recovery solution and since the nucleated cell diluted layer is plasma (see above), it would have been obvious to one of skill in the art to use such a layer to achieve the predictable result of recovering the nucleated cells.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Applicants notes that, in claim 1, the layer rich in unnecessary cells is first introduced into the filter device, followed by the layer rich in nucleated cells is then introduced therein, so as to recover the nucleated cells. The following advantages exist in a system in which the cell-containing solution is separated into a layer that is rich in nucleated cells and a layer that is rich in unnecessary cells, the layer rich in unnecessary cells is first introduced into the filter device, and the layer rich in nucleated cells is then introduced therein. First, the unnecessary cells remaining on the filter can

be washed with the layer that is rich in nucleated cells. Thus, the amount of unnecessary cells remaining on the filter can be decreased, and the purity of the recovered nucleated cells is increased. Second, as compared with the case where an un-separated cell-containing solution is introduced into the filter device, the amount of liquid which is used for capturing the nucleated cells on the filter material can be decreased. The nucleated cells remain near the surface of the filter material and thus, the nucleated cells can be easily recovered.

Applicant submits that a person skilled in the art, trying to improve on methods for recovering nucleated cells, would normally avoid introducing unnecessary cells into the filter device, and would avoid introducing a layer rich in unnecessary cells that were separated into the filter device. Applicant submits that these features of the present invention are not taught or suggested by any of the cited art.

Applicant argues that neither Sumita nor Oka1 disclose or suggest that the value obtained by dividing the effective filtration area of the filter material by the thickness of the nucleated cell-capturing material packed is between 15 and 120 cm (claims 11-17). Applicant notes that this feature of the claims is a feature of the filter device, which is suitable for the method wherein the layer rich in unnecessary cells is first introduced into the filter device, and the layer rich in nucleated cells is then introduced therein, so as to recover the nucleated cells.

Applicant argues that the object of Oka1 is to provide a method for removing leukocytes, by which the remaining concentration of leukocytes in the leukocyte-containing blood preparation is 10^{-4} or less (column 7, lines 22-25). Oka1 does not

teach anything about a method for recovering captured leukocytes and about the recovery efficacy for leukocytes. The description that "the remaining rate of leukocyte is low, namely the capture rate of leukocyte is high," does not suggest that the captured nucleated cells can be efficiently recovered. Rather, since high capture rate of leukocytes implies strong adsorption of leukocytes to non-woven fabric, one skilled in the art would expect the recovery rate of leukocytes to be decreased, and would not attempt to use the filter of Oka 1 for recovering nucleated cells. For these reasons as well, a person of skill in the art would not combine the teachings of Sumita and Oka1, and these documents do not render obvious the present invention.

Applicant argues that each of Oka2, Fukuda, and Rubinstein is deficient for other reasons. Applicant argues that Oka2 discloses that leukocytes are filtered out after blood samples are separated into several blood components by centrifugation (paragraph 0005), but discloses nothing about preparing a cell concentrate wherein the layer rich in unnecessary cells is first introduced into the filter device, and the layer rich in nucleated cells is then introduced therein, so as to recover the nucleated cells. Thus, even if combined, Sumita, Oka1, and Oka2 fail to render obvious claims 1 and those dependent therefrom.

Applicant argues that Fukuda discloses a method of removing leukocytes from blood samples by forming a blood cell concentration gradient in a pooling unit before introducing blood into a filter for eliminating the leukocytes. However, the object of Fukuda is to improve the filtration performance of the filter, and to provide a method for filtration of blood, which can be easily operated, along with an automated filtration

device suitable for the method. Fukuda describes as an advantage that leukocytes can be efficiently removed and that platelets can be highly recovered, but does not disclose a method for recovering the nucleated cells captured by the filter material, and does not disclose that the nucleated cells can be efficiently recovered. Thus, even if combined, Sumita, Oka1, Oka22, and Fukuda fail to render obvious claims 1 and those dependent therefrom.

Applicant argues that, while Rubinstein discloses that leukocytes can be efficiently removed, the reference fails to disclose or suggest that nucleated cells can be recovered. In fact, one would expect from Rubinstein that the recovery rate for the leukocytes is decreased, since efficient removal of leukocytes implies strong adsorption of leukocytes to the non-woven fabric. Thus, even if combined, Sumita, Oka1, Oka2, Fukuda, and Rubinstein fail to render obvious claims 1 and 12 and those dependent therefrom.

Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

It is noted that, although Applicant states that the combination of Sumita, Oka1, Oka2, Fukuda, and Rubinstein fails to render the claimed invention *prima facie* obvious, Applicant argues the references individually and does not address the combination of references. In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the

rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Specifically, Applicant argues that none of Oka1, Fukuda, and Rubinstein teaches a method for recovering captured leukocytes and that Oka2 does not teach preparing a cell concentrate wherein the layer rich in unnecessary cells is first introduced into the filter device, and the layer rich in nucleated cells is then introduced therein, so as to recover the nucleated cells. However, none of the references has to teach each and every claim limitation. If they did, this would have been anticipation and not an obviousness-type rejection. Apart from arguments, Applicant did not provide any evidence indicating that the above references cannot be combined.

Applicant argues that, the teaching of high capture rate of leukocytes in Oka1 and Rubenstein implies strong adsorption of leukocytes to the filter, and therefore, one skilled in the art would expect the recovery rate of leukocytes to be decreased, and would not attempt to use the filter of Oka1 or Rubinstein for recovering nucleated cells. This assertion is not found persuasive because it is not supported by any evidence. The instant separation is also based on high retention rate on non-woven fabric; does this mean that cells cannot be recovered from the instant non-woven filters? In fact, high retention rate does not equal decreased recovery. Applicant provided no evidence of strong adsorption to non-woven filters and there is no such teaching in Oka1 or Rubinstein. The instant specification discloses that any material can be used as a filter material as long as it is insoluble in water, i.e., there is no strong adsorption regardless of the material used (p. 17, second full paragraph). Furthermore, Oka1 uses non-woven

fabric with the same fiber diameter and packing density as the claimed filter (see the rejection above). Clearly, the filter disclosed in Oka1 is suitable for cell recovery. Rubinstein was only cited for teaching HES.

Applicant submits that one of skill in the art would normally avoid introducing a layer rich in unnecessary cells into the filter device and that this feature is not taught or suggested by any of the cited art. This is incorrect. As indicated in the rejection above, both Oka2 and Fukuda teach this feature. Applicant did not provide any evidence that one of skill in the art would not know how to apply such teachings to Sumita's method.

For the reasons set forth above, Applicant's arguments are not found persuasive and the rejection is maintained.

7. Claims 1-18 and 30-33 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Sumita et al. taken with each Oka et al. (U.S. Patent NO 5,298,165), Fukuda et al., Oka et al. (PGPUB 2004/0251195), and Rubinstein et al., in further view of Tanaka et al. (U.S. Patent No. 6,048,464).

The teachings of Sumita et al., Oka et al. (U.S. Patent NO 5,298,165), Fukuda et al., Oka et al. (PGPUB 2004/0251195), and Rubinstein et al. are applied as above for claims 1-17 and 30-33. Sumita et al., Oka et al. (U.S. Patent NO 5,298,165), Fukuda et al., Oka et al. (PGPUB 2004/0251195), and Rubinstein et al. do not teach a filter made from a combination of non-woven fabric with a sponge-like structure (claim 18). However, at the time the invention was made, such combination filters were taught by the prior art. For example, Tanaka et al. teach a nucleated cell-capturing filter

comprising both a sponge-like structure and a non-woven fabric (Abstract, column 3, lines 19-46, column 6, lines 17-26). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Sumita et al., Oka et al. (U.S. Patent NO 5,298,165), Fukuda et al., Oka et al. (PGPUB 2004/0251195), and Rubinstein et al. by using a combination filter comprising both a sponge-like structure and a non-woven fabric to achieve the predictable result of capturing nucleated cells.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Applicant's arguments regarding Sumita, Oka1, Oka2, Fukuda, and Rubenstein are the same as above.

With respect to Tanaka, Applicant note that the object of this disclosure is to provide a filter device and method for removing leukocytes, wherein leukocytes can be removed from leukocyte-containing liquid, such as a whole-blood composition at a high removal rate for leukocytes, while loss of useful blood components is greatly suppressed (see column 3, lines 19-46). The advantage in Tanaka is that leukocytes which cause side effects can be very effectively removed, while maintaining high recovery rate of useful blood components (column 30, lines 59-63). In particular, Tanaka does not disclose a method for recovering nucleated cells captured by the filter material, and does not disclose that nucleated cells can be efficiently recovered. While Tanaka may state that leukocytes can be efficiently removed, this does not imply that

nucleated cells may be recovered. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the reasons set forth above. Again, this is an obviousness-type rejection, and therefore Tanaka does not have to teach each and every claim limitation. Applicant did no provide any evidence indicating why Tanaka's teaching cannot be applied to the method of Sumita, Oka1, Fukuda, Oka2, and Rubinstein. For these reasons, the rejection is maintained.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Primary Examiner, Art Unit 1633